Naphthoquinone Derivatives and Lignans from the Paraguayan Crude Drug "Tayï Pytá" (*Tabebuia heptaphylla*, Bignoniaceae)

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Z. Naturforsch. **58 c**, 495–501 (2003); received December 9, 2002/February 10, 2003

The Paraguayan crude drug "tayï pytá" is used to treat cancer, wounds and inflammation. It consist of the bark and trunkwood of *Tabebuia heptaphylla* (Bignoniaceae). A phytochemical study of the crude drug gave, in addition to previously described naphthoquinones and the known lignans cycloolivil and secoisolariciresinol, three new lapachenol (lapachonone)-, two naphthofuran-, a chromone and a naphthalene derivative. The structures were elucidated by means of high field NMR spectroscopy. The biological activity of the main compound lapachol and the related α-lapachone as well as the lignans cycloolivil and secoisolariciresinol can explain, at least in part, the effect atributed to the crude drug in Paraguayan folk medicine.

Key words: Tabebuia heptaphylla, Bignoniaceae, Naphthoquinones

Introduction

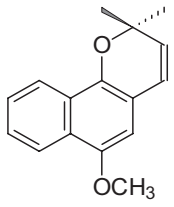
Tabebuia heptaphylla (Vell. Conc.) Toledo (Bignoniaceae) is a tree some 25–40 m tall with a stem diameter of 0.7–1.3 m. It is known under the common name "tayï pytá" or "lapacho" and is common in Eastern Paraguay. The wood or stem bark of *Tabebuia heptaphylla* (syn. *T. ipe* Standl.) and other Bignoniaceae trees is traditionally used in Paraguay and other South American countries to treat wounds, cancer and inflammations (Gupta, 1995; Bernal and Correa, 1989; Ortega Torres *et al.*, 1989).

Several studies have been performed on the chemistry of *Tabebuia* and the close related *Tecoma* species as well as on the biological activity of their naphthoquinone derivatives (Hegnauer, 1989; Hegnauer, 1964). Since there is an important source of "lapacho" sawdust mainly in Paraguay, southern Brazil and northeastern Argentina, a study was carried out to isolate and identify the secondary metabolites from a Paraguayan sample of the crude drug. We now report on the isolation of naphthoquinones and lignans from the wood of *Tabebuia heptaphylla.*

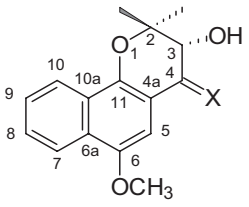
Results and Discussion

The trunkwood extract of *T. heptaphylla* afforded in addition to the known lapachenol (lapachonone) (**1**), lapachol (**5**), α-lapachone (**6**), Rhinacantin A (**7**), Stenocarpone B (**8**) (Stenocarpoquinone), Avicequinone A (**9**), dehydro-α-lapachone (**13**), dehydroiso-α-lapachone (**14**), Stenocarpoquinone A (**15**) and the lignans secoisolariciresinol (**16**) and cycloolivil (**17**), the new lapachenol derivatives (**2**–**4**), the naphthalene derivative (**10**), the chromone (**11**) and the naphthofurans (**12**) and (**18**).

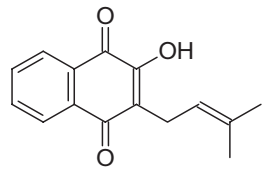
The high resolution MS of **2** calculates $C_{16}H_{18}O_3$ for the molecular ion at *m/z* 258. The ^{1}H-NMR spectrum of **2** (Table I) was close to that of **1** differing mainly in signals for the heterocyclus. Instead of the pair of doublets observed for the 3-H and 4-H in **1**, three dd at δ 2.85, 3.17 and 3.68 ppm appeared. The latter, assignable to the proton geminal to hydroxy group was shifted downfield (δ 5.10) on acetylation indicating a -CHOH-CH_2- sequence and a hydroxy derivative of **1**. The position of the OH group at C-3 was deduced on the basis of chemical shift of the C**H**OH signal. In the MS of **3** the $[M]^+$ peak at *m/z* 274 ($C_{16}H_{18}O_4$) indicated an additional hydroxy group. This assumption was con-



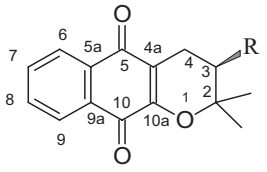
1 Lapachenol
(Lapachonone)



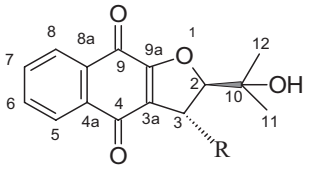
X
2 H_2
3 βOH, H
4 O



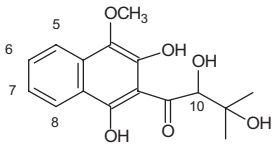
5 Lapachol



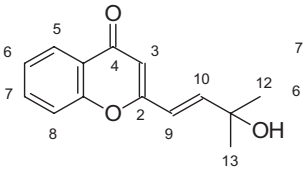
R
6 H α-Lapachone
7 OH Rhinacantin A



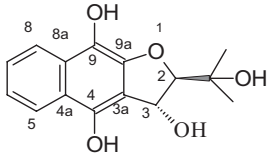
R
8 H Stenocarpone B
9 OH Avicequinone A



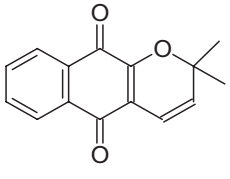
10



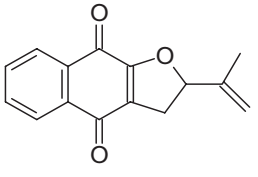
11



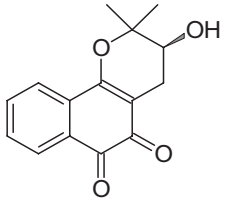
12



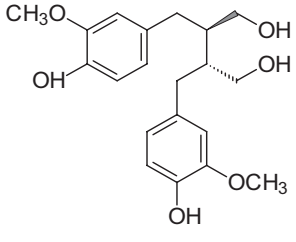
13 Dehydro-α-lapachone



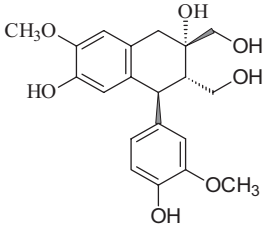
14 Dehydroiso-α-lapachone



15 Stenocarpoquinone A



16 Secoisolariciresinol



17 Cycloolivil

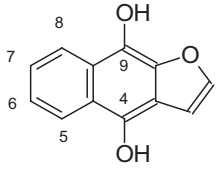


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Fig. 1. Naphthoquinone derivatives and lignans isolated from *Tabebuia heptaphylla* wood.

Table I. ^{1}H-NMR spectral data of compounds **2**–**4** and **7**–**9** in $CDCl_3$, δ H in ppm (*J* in Hz) (400 MHz).

H	**2**	**2** Ac	**3**	**4**	**7**	**8**	**9**
2	–	–	–	–	–	4.93 dd	4.52 d
3	3.68 dd	5.10 dd	3.74 d	4.54 d	3.92 dd	3.07 dd	5.60 d
3′	–	–	–	–	–	3.13 dd	–
4	2.85 dd	2.84 dd	4.67 d	–	2.63 dd	–	–
4′	3.17 dd	3.23 dd	–	–	2.83 dd	–	–
5	6.46 s	6.43 s	6.77 s	7.03 s	–	7.88 dd	8.02 dd
6	–	–	–	–	7.84 dd	7.67 ddd	7.67 ddd
7	8.15 m	8.15 m	8.16 m	8.23 dd	7.53 ddd	7.88 ddd	7.72 ddd
8	7.49 m	7.48 m	7.50 m	7.58 dd	7.66 ddd	8.09 dd	8.05 dd
9	7.46 m	7.45 m	7.50 m	7.66 dd	8.07 dd	–	–
10	8.16 m	8.16 m	8.16 m	8.28 dd	–	–	–
C-2 Me	1.36 s	1.38 s	1.59 s	1.78 s	1.52 s	1.41 s	1.40 s
C-2 Me	1.46 s	1.41 s	1.28 s	1.28 s	1.46 s	1.28 s	1.33 s
OMe	3.94 s	3.94 s	3.99 s	4.00 s	–	–	–
OAc	–	2.08 s	–	–	–	–	–
OH				3.82 d			

J (Hz): **2**: 3,4 = 3,4′= 5; 4,4′ = 17.5. **2Ac**: ; 3,4 = 3,4′= 5; 4,4′ = 18.5. **3**: 3,4 = 8. **4**: 3, OH = 6. **7**–**9**: 7,8 = 8,9 = 9,10 = 7.5; 7,9 = 8,10 = 1.5; **7**: 3,4 = 3,4′ = 5; 4,4′= 18; **8**: ; 2,3 = 8.5; 2,3′= 10; 3,3′ = 15; **9**: 2,3 = 5.

firmed by a pair of doublets at δ 3.74 and δ 4.67 in the ^{1}H-NMR spectrum (Table I) and two doublets at δ 77.19 and 78.34 in the ^{13}C-NMR spectrum (Table II). The stereochemistry was deduced from NOE difference experiments. One of C-2 methyl groups showed strong interactions with H-4 while the other one with H-3 indicating *trans* orientation of the hydroxy groups. The position of the methoxy group was deduced from the NOE effects between H-5, H-4 (2%) and OMe (7%). The compound **4** showed the $[M]^+$ at *m/z* 272 (calc. for $C_{16}H_{16}O_4$). The ^{1}H-NMR spectrum (Table I) was close to that of **2** and **3**, differing mainly in the lack of the H-4 signal. Thus a 4-oxo derivative was established. The position of the keto group follows from the chemical shift of the H-3 signal. The ^{1}H-NMR data of compounds **7**–**9** is presented in Table I.

Table II. ^{13}C NMR spectral data of compounds **3**, **7**, **9** and **11** in $CDCl_3$ (100.6 MHz).

C	**3**	**7**	**9**	**11**
2	70.08 s	81.33 s	71.68 d	161.4 s
3	77.19 d	68.35 d	98.60 d	146.45 d
3a	–	–	124.72 s	
4	78.34 d	25.42 t	178.14 s	196.53 s
4a	101.65 s	110.30 s	132.82 s	105.8 s
5	115.35 d	178.74 s	133.28 d	125.6 d
5a	–	132.01 s	–	
6	141.15 s	130.95 d	126.12 d	124.9 d
6a	126.17 s	–	–	
7	125.91 d	124.33 d	126.53 d	119.58 d
8	121.67 d	128.78 d	134.51 d	117.74 d
8a	–	–	131.62 s	123.98 s
9	122.06 d	134.87 d	182.67 s	133.63 d
9a	–	130.08 s	160.78 s	
10	125.99 d	179.46 s	72.84 s	110.48 d
10a	125.68 s	161.39 s	–	
11	149.46 s	–	–	71.16 s
Me	26.49 q	22.07 q	25.54 q*	29.72 q
Me	18.67 q	25.04 q	24.59 q*	29.72 q
OMe	55.68 q	–	–	

* May be interchangeable.

The presence of a 1,4-dihydroxynaphthol nucleus with no substituents on the aromatic ring in compounds **10**, **12** and **18** (Table III) was suggested by the ^{1}H-NMR spectrum which showed the typical coupling patterns for an AA′BB′ system for the aromatic ring.

The high resolution of the molecular ion at *m/z* 306 in the MS of compound **10** calculates for $C_{16}H_{18}O_6$ and indicates eight degrees of unsaturation. The fragment at *m/z* 175 in the MS calculates for $C_{10}H_7O_3$ indicating that three oxigen functions have to be placed in the ring moiety while the loss of 59 units at *m/z* 247 pointed out to the loss of C_3H_7O of the side chain. The ^{1}H-NMR spectrum showed the typical coupling patterns for an AA′BB′ system for the aromatic ring, a methoxy group, two methyl singlets at δ 1.53 and a doublet at δ 4.67. The nature of the oxygen functions was deduced from the NMR data (Table III) and complemented with the fragmentation pattern in the MS, leading to the naphthalene derivative **10**.

Table III. ^{1}H-NMR spectral data of compounds **10**, **11**, **12** and **18** in $CDCl_3$, δ H in ppm (*J* in Hz) (400 MHz).

H	10	11	12	18
2			4.64 d (4)	7.52 d (2)
3	–	6.24 s	5.51 d (4)	6.89 d (2)
5	8.06 dd	8.18 dd	7.76 dd (7.5;1.5)	7.74 dd (8;1)
6	7.62 dd	7.67 ddd	7.64 ddd (7.5;7.5;1.5)	7.49 ddd (8;8;1)
7	7.57 ddd	7.39 ddd	7.70 ddd (7.5;7.5;1.5)	7.67 ddd (8;8;1)
8	7.41 dd	7.48 dd	8.11 dd (7.5;1.5)	8.10 dd (8;1)
9	–	6.92 d	–	–
10	4.67 d (6)	6.42 d	–	–
11			1.37 s	–
12			1.43 s	–
Me	1.53 s	1.47 s		
Me	1.53 s	1.47 s		
OMe	3.87 s	–		
OH	3.77 brs	–		

J (Hz) **10** and **11**: 5,6 = 6,7 = 7,8 = 7.5; 5,7 = 6,8 = 1.5; 9,10 = 16.

The ^{1}H-NMR data of **11** (Table III) showed the typical coupling patterns for an AA′BB′ system for the aromatic ring, a conjugated *trans*-double bond, a singlet at δ 6.24 and two methyl singlets at δ 1.47. The placement of the side chain at C-2 followed from the chemical shift of the H-3 signal and is in agreement with a chromone derivative. The ^{13}C-NMR spectrum (Table II) and the MS with the molecular ion at *m/z* 230 (calc. for $C_{14}H_{14}O_3$) confirmed the structure.

The molecular formula of compound **12** ($C_{15}H_{16}O_5$) indicates eight degrees of unsaturation. The ^{1}H-NMR spectrum (Table III) was similar to that of **9** and presented two methyl singlets at δ 1.43 and 1.37 as well as a pair of doublets at δ 4.64 and 5.51 with J = 4 Hz, indicating a 2-(1-hydroxy-1-methylethyl)-3-hydroxydihydrofuran ring with the same configuration at C-2 and C-3 than in compound **9**. The ^{1}H-NMR data are in agreement with the proposed structure. Compound **12** is related to avicenol-A, its dimethoxy derivative reported by Ito *et al.* (2000) from *Avicennia alba.*

The structure of compound **18** followed from the ^{1}H-NMR spectrum (Table III) and the molecular formula $C_{12}H_8O_3$. Instead of the two methyl singlets and the pair of doublets for the 2-(1-hydroxy-1-methylethyl)-3-hydroxydihydrofuran ring, two doublets at δ 7.52 and 6.89 with J = 2 Hz coupled to each other pointed out to a furan ring. The corresponding dimethoxy derivative, known as Avicenol-B has been reported by Ito *et al.* (2000).

Lapachonone (lapachenol) (**1**) has been reported as a constituent of the heartwood of *Tabebuia avellanedae*, *Paratecoma alba*, *P. peroba* and *Tectona grandis* (Dictionary of Natural Products on CD-ROM, 2002, Hegnauer, 1989; 1964). Related compounds have been reported from *Tabebuia avellanedae* (Wagner *et al.*, 1989).

α-Lapachone (**6**) was previously isolated from the wood of the Bignoniaceae trees *Tabebuia avellanedae*, *T. guayacan* and *T. pentaphylla* as well as from *Catalpa ovata*, *Haplophragma adenophyllum* and *Zeyhera tuberculosa* (Dictionary of Natural Products, 2002; Weinberg *et al.*, 1976). Its 4S-hydroxy-9-methoxy (Itokawa *et al.*, 1992) as well as 4-oxo-9-methoxy-α-lapachone (Fujiwara *et al.*, 1998) shows antitumor-promoting activity. The close related dehydro-α-lapachone **13** was reported from *Markhamia platycalyx*, *Paratecoma peroba*, *Tabebuia rosea*, *T. palmeri*, *T. pentaphylla* and *Radermachia sinica.* Dehydroiso-α-lapachone (**14**) is a common constituent in Bignoniaceae wood. It has been reported from *Markhamia platycalyx*, *Radermachia sinica*, *Tabebuia rosea*, *T. pentaphylla* and *Paratecoma peroba*.

Rhinacanthin A **7** was first reported as a constituent of *Rhinacanthus nasutus* roots. While the close related ester Rhinacanthin B, bearing a 10-carbon unit side chain was cytotoxic, the Rhinacanthin A was inactive, showing the contribution of the ester chain to cytotoxicity (Wu *et al.*, 1998; Wu *et al.*, 1988). Stenocarpone B (**8**) (stenocarpoquinone) was first isolated from *Stenocarpus salignus.* The 3-hydroxy derivative (**9**), known as avicequinone A was reported as a constituent from *Avicennia alba* by Ito *et al.* (2000) and Itoigawa *et al.* (2001). According to Itoigawa *et al.* (2001), avicequinone A inhibits the effect on mouse skin tumor promotion in an *in vivo* carcinogenesis test. Furthermore, Ito *et al.* (2000) re-

ported the quinone as a phytoalexin. Avicenol A which is closely related to compound **12** was reported as a constituent of the stem bark of *Avicenia alba* (Ito *et al.*, 2000). Stenocarpoquinone A (**15**) has been isolated for the first time from *Stenocarpus salignus* (Dictionary of Natural Products on CD-ROM, 2002).

The lignans secoisolariciresinol and cycloolivil were isolated from the sample under study. Secoisolariciresinol (**16**) and their derivatives were reported from several plant species, including *Cedrus deodara* (Agrawal and Rastogi, 1982), *Virola sebifera* (Martinez *et al.*, 1999) and *Rubus amabilis* (Chen *et al.*, 2000). Cycloolivil (**17**) has been reported as a constituent of *Olea cunninghamii*, *Gmelina asiatica* and *Gymnelaea cunninghamii.* Its 6-*O*-β-D-glucoside was isolated from *Osmanthus asiaticus* (Sugiyama *et al.*, 1993).

Biological activity

"Lapacho" wood chips are widely traded as a crude drug in Paraguay, Brazil and Argentina. The composition of the drug is relevant for standardization of preparations and requires isolation and identification of their constituents. The main compounds isolated from the Paraguayan sample of "lapacho" were lapachol, lapachonone (lapachenol), α-lapachone and its isomers. Furthermore, two known lignans were isolated and identified.

Biological activities reported for lapachol and its derivatives comprises molluscicidal (Santos *et al.*, 2001) and trypanocidal effect (Santos *et al.*, 2001; Pinto *et al.*, 2000) as well as interceptive activity (Guerra *et al.*, 1999). Lapachol has been shown to display weak activity against the amastigote form of the parasite *Leishmania donovani* in peritoneal mice macrophages. The proposed mechanism of action is based on the generation of oxygen free radicals (Chan-Bacab and Peña-Rodriguez, 2001). In a study of differentiation-inducing agents, Dinnen and Ebusuzaki (1997) identified lapachol as the active compound from the crude drug "pau d'arco". As a vitamin K antagonist, lapachol might target such vitamin K-dependent reactions as the activation of a ligand for the Axl receptor tyrosine kinase. Other activities reported for lapachol comprises gastroprotective effect (Goel *et al.*, 1987), antifungal and antibacterial activity (Binutu *et al.*, 1996).

Lapachol and β-lapachone were investigated for their effect towards the protozoa *Trypanosoma cruzi*, which causes Chaga's disease in Latin America. The studies comprises both assays of the natural products as well as semisynthetic derivatives. Neves-Pinto *et al.* (2002) reported the promising effects of a phenazine derived from β-lapachone.

Furthermore, α- and β-lapachone are members of a new inhibitor class of cellular DNA topoisomerase II, and α-lapachone, in particular, can be considered a potential lead for the development of drugs to treat multidrug-resistant cell lines with lower expression of topoisomerase II (Krishnan and Bastow, 2001; Krishnan and Bastow, 2000).

In a study of the antioxidant activity of plant extracts, Lee *et al.* (1998) found that (+)-cycloolivil was the active principle from *Cerbera manghas* L. (Apocynaceae). The lignan was able to scavenge the free radical 1,2-diphenyl-2-picrylhydrazyl (DPPH) and to inhibit the 7,12-dimethylbenz(a) anthracene-induced preneoplastic lesion formation with a mouse mammary organ culture model.

Several biological activities have been related with plant lignans, including phytoestrogenic effects (Boker *et al.*, 2002), their role as precursors of mammalian lignans (Heinonen *et al.*, 2001), cancer chemopreventive activity of secoisolariciresinol diglucoside-hydroxymethyl glutaryl ester (Ford *et al.*, 2001) and antioxidant effect of secoisolariciresinol (Prasad, 2000).

Conclusions

Nine known and seven new naphthoquinone derivatives as well as two known lignans were isolated from the heartwood of *Tabebuia heptaphylla.* The main compounds were lapachenol (lapachonone) (**1**) and lapachol (**5**), both widespread constituents from *Tabebuia*, *Tecomella* and *Tectona* species. The new products **2**–**4** are oxidation derivatives from lapachenol. Compounds **12** and **18** are related to avicenol A and avicenol B, the corresponding methyl ethers isolated from *A. alba* by Ito *et al.* (2000). The compounds **2**–**4**, **10**–**12** and **18** are reported for the first time in this work.

The biological activities reported for lapachol and α-lapachone as well as the antioxidant effect of the lignans isolated from the sample give a rationale for the use of "lapacho" wood in Paraguayan tradi-

tional medicine. Furthermore, the sawdust residues of the wood industry can be used as a source of crude lapachol and lapachenol at low cost.

Materials and Methods

Plant material

Tabebuia heptaphylla wood was purchased in Asunción on November 1991. Wood specimens are deposited at the Herbario de la Universidad de Talca, Chile.

Isolation of the compounds

Wood chips (4.5 kg) were extracted three times with EtOAc (3 × 10 l) at room temperature for one week. The resulting extract was filtered and concentrated to a syrup under reduced pressure. The crude extract was treated with CH_2Cl_2 (4 × 2 l), affording 45.64 g of CH_2Cl_2-solubles and 107 g of crude lapachol. Further 150 g of CH_2Cl_2-insolubles were obtained. The CH_2Cl_2-soluble fraction (45.64 g) was chromatographed on silica gel (400 g) with a petrol to EtOAc gradient. Thirty-five fractions of 200 ml each were collected. Fractions 1–6 afforded 46 g lapachonone (lapachenol) (**1**). Fractions 7–13 yielded 4 g lapachol (**5**) (Thomson, 1987) while fractions 14–18 contained 250 mg dehydro-α-lapachone (**13**), 300 mg dehydroiso-α-lapachone (**14**) and further 1.6 g **5**. Fraction 19 afforded after repeated TLC (silica gel; PE: CH_2Cl_2 3:7 v/v) 1 g **5** and 6 mg **4**. From the fractions 20–21, after repeated TLC (a) CH_2Cl_2; (b) CH_2Cl_2: EtOAc 9:1 v/v; (c) CH_2Cl_2: EtOAc 4:1 v/v; 6 mg **2**, 6 mg **3**, 5 mg **4**, 5 mg **6**, 8 mg **7**, 4 mg stenocarpoquinone A (**15**) and 1 mg **18** were obtained. Fraction 22–24 yielded after repeated TLC (a) CH_2Cl_2; (b) CH_2Cl_2: EtOAc 9:1 v/v; CH_2Cl_2: EtOAc 4:1 v/v, 2 mg **3**, 2 mg stenocarpoquinone B (**8**), 8 mg **9** and 2 mg **12**. Fractions 25–28 afforded after TLC (CH_2Cl_2: EtOAc 9:1 v/v (3 ×) and EtOAc) four bands. After TLC, 2 mg **3** and 1.5 mg **8** were isolated from the band 2, while band 3 afforded after HPLC (RP-8; MeOH:H_2O 5.5:4.5 v/v), 1.5 mg **9** (Rt 4.5 min), 2 mg **10** (Rt 5.5 min) and 2 mg **11** (Rt 8.0 min). Fractions 29/35 yielded after TLC (CH_2Cl_2: EtOAc 4:1 v/v (3 ×)), 10 mg secoisolariciresinol (**16**) and 15 mg (+)-cyclo-olivil (**17**).

Mass spectra (MS): ionization energy: 70 eV. ^{1}H-NMR spectra: 400 MHz, ^{13}C-NMR: 100.6 MHz, $CDCl_3$ as solvent. Known compounds were identified on comparison of the spectral data with literature.

2,2-Dimethyl-3-hydroxy-3,4-dihydro-6-methoxy-4H-naphtho[1,2-b]pyran (**2**). Colorless resin, MS: *m/z* (rel. int.): 258.126 (calc. for $C_{16}H_{18}O_3$: 258.126) (91); 225 (66); 202 (80); 187 (100); 186 (94); 173 (22); 159 (34); 128 (40); 115 (50); 57 (72).

2,2-Dimethyl-3α,4β-dihydroxy-3,4-dihydro-6-methoxy-4H-naphtho [1,2-b]pyran (**3**). Colorless resin, MS: *m/z* (rel. int.): 274.120 (calc. for $C_{16}H_{18}O_4$: 274.120) (44); 202 (RDA) (100); 187 (50); 57 (44).

2,2-Dimethyl-3-hydroxy-3α,4β-dihydro-4-oxo-6-methoxy-4H-naphtho[1,2-b]pyran (**4**). Colorless resin, MS: *m/z* (rel. int.): 272.105 (calc. for $C_{16}H_{16}O_4$: 272.105); 200 RDA (C_4H_8O) (72)

2,3-Dihydro-3-hydroxy-2-(1-hydroxy-1-methyl-ethyl)naphtho [2,3-b] furan-4,9-dione (**9**). Colorless resin, MS: *m/z* (rel. int.): 274.084 (calc. for $C_{15}H_{14}O_5$: 274.084) $[M]^+$ (16); 256 (8); 241 (98); 216 (89) $[M\text{-}58]^+$; 203 (34); 202 (68); 199 (72); 198 (64); 187 (44); 173 (95); 149 (68); 105 (66); 73 (88); 59 (100); 57 (90).

2,4-Dihydroxy-3-(2,3-dihydroxy-3-methyl-1-oxo-butyl)-1-methoxynaphthalene (**10**). Colorless resin, MS: *m/z* (rel. int.): 306.110 (calc. for $C_{16}H_{18}O_6$: 306.110) $[M]^+$ (0.8); 247 (56); 235 (50); 203 (78); 175 ($C_{10}H_7O_3$)(100); 163 (82); 72 (72); 59 (75); 57 (73).

2-(3-Hydroxy-3-methylbut-1-enyl)-4-oxo-4H-chromone (**11**). Colorless resin, MS: *m/z* (rel. int.): 230.094 (calc. for $C_{14}H_{14}O_3$: 230.094) $[M]^+$ (14); 215 (28); 187 (100); 173 (44); 149 (8); 121 (42); 57 (34)

2,3-Dihydro-2-(1-hydroxy-1-methylethyl)-3,4,9-trihydroxynaphtho [2,3-b] furan (**12**). Colorless resin, MS: *m/z* (rel. int.): 276.099 (calc. for $C_{15}H_{16}O_5$: 276.0997) $[M]^+$ (1); 200 (18); 175 (20); 151 (25); 138 (48); 137 (100); 105 (30); 59 (46); 57 (44).

4,9-Dihydroxynaphtho[2,3-*b*] furan (**18**). Colorless resin, MS: *m/z* (rel. int.): 200.047 $[M]^+$ (calc. for $C_{12}H_8O_3$: 200.047) (25); 149 (64); 131 (80); 57 (100).

Acknowledgements

The financial support from the Dirección de Investigación, Universidad de Talca and the International Foundation for Science (I. F. S., Grant F-928-3F) is gratefully acknowledged.

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